

AMENDMENTS TO THE CLAIMS

Please amend the claims as follows:

This listing of claims will replace all prior versions, and listing, of claims in the application:

Claim 1 (currently amended): A method for treatment of heart failure comprising ~~attenuating PLB-induced cardiac SR Ca^{2+} -ATPase (SERCA2a) inhibition and enhancing contractility in a heart comprising~~ (a) providing a compound comprising an exogenous dominant negative phospholamban (PLB) protein functionally attached to a transport peptide or a vesicle-based transfer system; and (b) contacting the heart with the compound, thereby ~~attenuating PLB-induced cardiac SR Ca^{2+} -ATPase (SERCA2a) inhibition and enhancing contractility in a heart to treat~~ treating the heart failure.

Claims 2 and 3 (canceled)

Claim 4 (previously presented): The method of claim 19, wherein the mutations of PLB comprise sense mutations.

Claims 5 to 11 (canceled)

Claim 12 (currently amended): A method for treatment of heart failure comprising enhancement of cardiac contractility by inhibition of phospholamban (PLB)- sarcoplasmic reticulum calcium ATPase (SERCA2a) interaction comprising

(a) providing an exogenous dominant negative PLB protein functionally attached to a transport peptide or a vesicle-based transfer system; and

(b) delivering an effective amount of the compound to cardiac tissue to inhibit interaction between PLB and SERC2a, thereby inhibiting wild-type PLB-sarcoplasmic reticulum calcium ATPase (SERCA2a) interaction and enhancing cardiac contractility and treating heart failure.

Claims 13 to 15 (canceled)

Claim 16 (previously presented): The method of claim 22, wherein the mutations of PLB comprise sense mutations of PLB.

Claims 17 and 18 (canceled)

Claim 19 (currently amended): The method of claim 1 [[19]], wherein the exogenous dominant negative PLB protein comprises a PLB protein with mutations.

Claim 20 (currently amended): The method of claim 1 [[19]], wherein the exogenous dominant negative PLB protein comprises a truncated PBL protein.

Claim 21 (canceled)

Claim 22 (previously presented): The method of claim 12, wherein the exogenous dominant negative PLB protein comprises a PLB protein with mutations.

Claim 23 (previously presented): The method of claim 12, wherein the exogenous dominant negative PLB protein comprises a truncated PBL protein.

Claim 24 (withdrawn): A method for attenuating phospholamban (PLB)-induced cardiac SR Ca^{2+} ATPase (SERCA2a) inhibition in a heart cell or a muscle cell, comprising

(a) providing a compound comprising an expression construct comprising a coding sequence for a dominant negative PLB functionally linked to a promoter active in the heart or the muscle cell, and the dominant negative PLB binds to wild-type PLB; and

(b) contacting the heart cell or the muscle cell with an effective amount of the compound, thereby attenuating phospholamban (PLB)-induced cardiac SR Ca^{2+} ATPase (SERCA2a) inhibition in the heart cell or the muscle cell.

Claim 25 (withdrawn): A method for increasing cardiac SR Ca^{2+} ATPase (SERCA2a) activity in a heart cell or a muscle cell,

(a) providing a compound comprising an expression construct comprising a coding sequence for a dominant negative phospholamban (PLB) functionally linked to a promoter active in the heart or the muscle cell, and the dominant negative PLB binds to wild-type PLB in the heart or the muscle cell; and

(b) contacting the heart cell or the muscle cell with an effective amount of the compound, thereby attenuating PLB-induced SERCA2a inhibition and increasing SERCA2a activity in the cell.

Claim 26 (withdrawn): The method of claim 24 or claim 25, wherein the heart cell is a cardiac myocyte.

Claim 27 (withdrawn): The method of claim 24 or claim 25, wherein the muscle cell is a smooth muscle cell.

Claim 28 (withdrawn): The method of claim 24 or claim 25, wherein the contacting is *in vitro*.

Claim 29 (withdrawn): The method of claim 24 or 25, wherein the contacting is *in vivo*.

Claim 30 (withdrawn): The method of claim 24 or 25, wherein the expression construct comprising a coding sequence for a dominant negative PLB further comprises a coding sequence for a penetratin peptide.

Claim 31 (withdrawn): A method for enhancing contractility in a heart comprising

(a) providing a compound comprising an expression construct comprising an expression construct comprising a coding sequence for a dominant negative phospholamban (PLB)

functionally linked to a promoter active in the heart, and the dominant negative PLB binds to wild-type PLB; and

(b) contacting the heart with an effective amount of the compound, thereby attenuating PLB-induced cardiac SR Ca^{2+} ATPase (SERCA2a) inhibition and enhancing contractility in the heart.

Claim 32 (withdrawn): A method for increasing heart activity comprising

(a) providing a compound comprising an expression construct comprising a coding sequence for a dominant negative phospholamban (PLB) functionally linked to a promoter active in the heart, and the dominant negative PLB binds to wild-type PLB; and

(b) contacting the heart with an effective amount of the compound, thereby attenuating PLB-induced cardiac SR Ca^{2+} ATPase (SERCA2a) inhibition and increasing heart activity.

Claim 33 (withdrawn): A method for treating heart failure comprising

(a) providing a compound comprising an expression construct comprising a coding sequence for a dominant negative phospholamban (PLB) functionally linked to a promoter active in the heart, and the dominant negative PLB binds to wild-type PLB; and

(b) contacting the heart with an effective amount of the compound, thereby attenuating PLB-induced cardiac SR Ca^{2+} ATPase (SERCA2a) inhibition, enhancing contractility or relaxation in the heart and treating the heart failure.

Claim 34 (withdrawn): The method of claim 31, claim 32 or claim 33, wherein the expression construct comprises an adenoviral expression construct.

Claim 35 (withdrawn): The method of claim 31, claim 32 or claim 33, wherein the dominant negative phospholamban (PLB) has an altered amino acid sequence as compared to wild-type PLB.

Claim 36 (withdrawn): The method of claim 31, claim 32 or claim 33, wherein the dominant negative phospholamban (PLB) is a truncated PLB.

Claim 37 (withdrawn): The method of claim 36, wherein the truncated PLB comprises SEQ ID NO:8.

Claim 38 (withdrawn): The method of claim 36, wherein the truncated PLB comprises a PLB cytoplasmic domain.

Claim 39 (withdrawn): The method of claim 31, claim 32 or claim 33, wherein the dominant negative phospholamban (PLB) has an altered amino acid sequence as compared to wild-type PLB.

Claim 40 (previously presented): The method of claim 1 or claim 12, wherein the exogenous dominant negative PLB protein is linked to the transport peptide by a covalent linkage.

Claim 41 (previously presented): The method of claim 40, wherein the covalent linkage comprises a polylysine, a single peptide bond or a disulfide bond.

Claim 42 (previously presented): The method of claim 41, wherein the polylysine comprises a branched polylysine.

Claim 43 (currently amended): The method of claim 1 or claim 12 [[40]], wherein the transport peptide comprises an antennapedia transport peptide or a penetratin.

Claim 44 (currently amended): The method of claim 43 [[40]], wherein the antennapedia transport peptide comprises SEQ ID NO:7.

Claim 45 (previously presented): The method of claim 1 or claim 12, wherein the exogenous dominant negative PLB protein comprises the first 16 residues of SEQ ID NO:8; SEQ ID NO:17; SEQ ID NO:18; or SEQ ID NO:19.

Claim 46 (new): A method for increasing heart activity or treating heart failure comprising attenuating phospholamban (PLB)-induced cardiac SR Ca^{2+} ATPase (SERCA2a) inhibition and enhancing contractility in a heart comprising (a) providing a compound comprising an exogenous dominant negative PLB protein functionally attached to a transport peptide or a vesicle-based transfer system, wherein the dominant negative PLB acts as a competitive inhibitor of endogenous phospholamban interactions with SERCA2a or the dominant negative PLB binds to wild-type PLB; and (b) contacting the heart with the compound, thereby attenuating wild-type PLB-induced cardiac SR Ca^{2+} ATPase (SERCA2a) inhibition and enhancing contractility in a heart to treat the heart failure.

Claim 47 (new): A method for increasing heart activity or treating heart failure comprising attenuating phospholamban (PLB)-induced cardiac SR Ca^{2+} ATPase (SERCA2a) inhibition and enhancing contractility in a heart comprising (a) providing a compound comprising an exogenous dominant negative PLB protein functionally attached to a means for internalization of the compound through a cell membrane into a cytoplasm, wherein the dominant negative PLB acts as a competitive inhibitor of endogenous phospholamban interactions with SERCA2a; and (b) contacting the heart with the compound, thereby attenuating wild-type PLB-induced cardiac SR Ca^{2+} ATPase (SERCA2a) inhibition and enhancing contractility in a heart to treat the heart failure.

Claim 48 (new): A method for treatment of heart failure comprising attenuating phospholamban (PLB)- induced cardiac SR Ca^{2+} ATPase (SERCA2a) inhibition and enhancing contractility in a heart comprising (a) providing a compound comprising an exogenous dominant negative PLB protein functionally attached to a transport peptide or a vesicle-based transfer system, wherein the dominant negative PLB binds to wild-type PLB; and (b) contacting the heart with the

compound, thereby attenuating wild-type PLB-induced cardiac SR Ca^{2+} ATPase (SERCA2a) inhibition and enhancing contractility in a heart to treat the heart failure.

Claim 49 (new): The method of claim 1 or claim 12, wherein the transport peptide comprises a receptor-independent transport mechanism.

Claim 50 (new): The method of claim 49, wherein the receptor-independent transport mechanism comprises a lipid vesicle based transfer.

Claim 51 (new): The method of claim 1 or claim 12, wherein the vesicle-based transfer system comprises an adenoviral-based transfer system.

Claim 52 (new): The method of claim 1 or claim 12, wherein the transport peptide is selected from the group consisting of a penetratin, an adenovirus, a bacterial and a lipid vesicle-based transport peptide.

Claim 53 (new): The method of claim 19, wherein the mutated exogenous dominant negative form of phospholamban (PLB) comprises a mutation at amino acid residue 16 from serine (S) to glutamic acid (E) (S16E).

Claim 54 (new): The method of claim 22, wherein the mutated exogenous dominant negative form of phospholamban (PLB) comprises a mutation at amino acid residue 16 from serine (S) to glutamic acid (E) (S16E).

Claim 55 (new): The method of claim 19, wherein the mutated exogenous dominant negative form of phospholamban (PLB) comprises a mutation at amino acid residue 3 from lysine (K) to glutamic acid (E) and a mutation at amino acid residue 14 from arginine (R) to glutamic acid (E) (K3E/R14E).

Claim 56 (new): The method of claim 22, wherein the mutated exogenous dominant negative form of phospholamban (PLB) comprises a mutation at amino acid residue 3 from lysine (K) to glutamic acid (E) and a mutation at amino acid residue 14 from arginine (R) to glutamic acid (E) (K3E/R14E).